

FIGURE 1

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VIR501 and VIR502 third round plaque picks
IL2-ELISA testing of undiluted culture medium from T25 infections

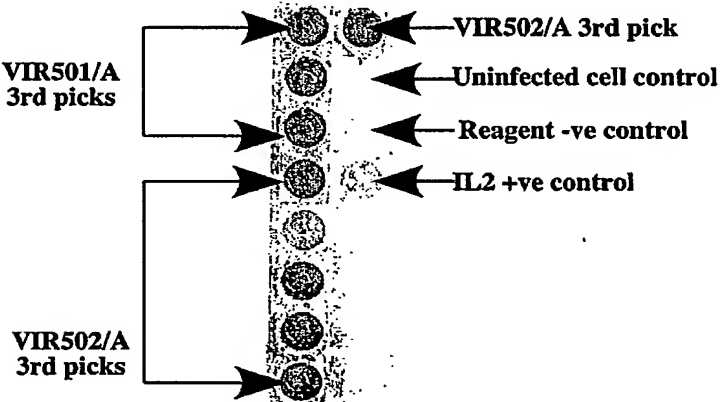


FIGURE 2

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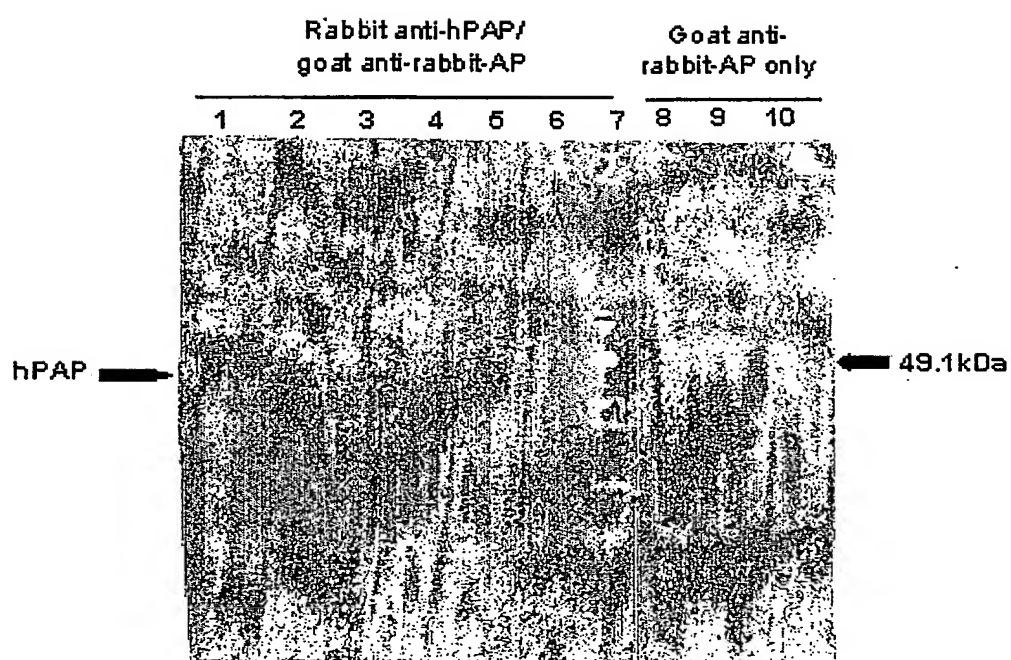


FIGURE 3

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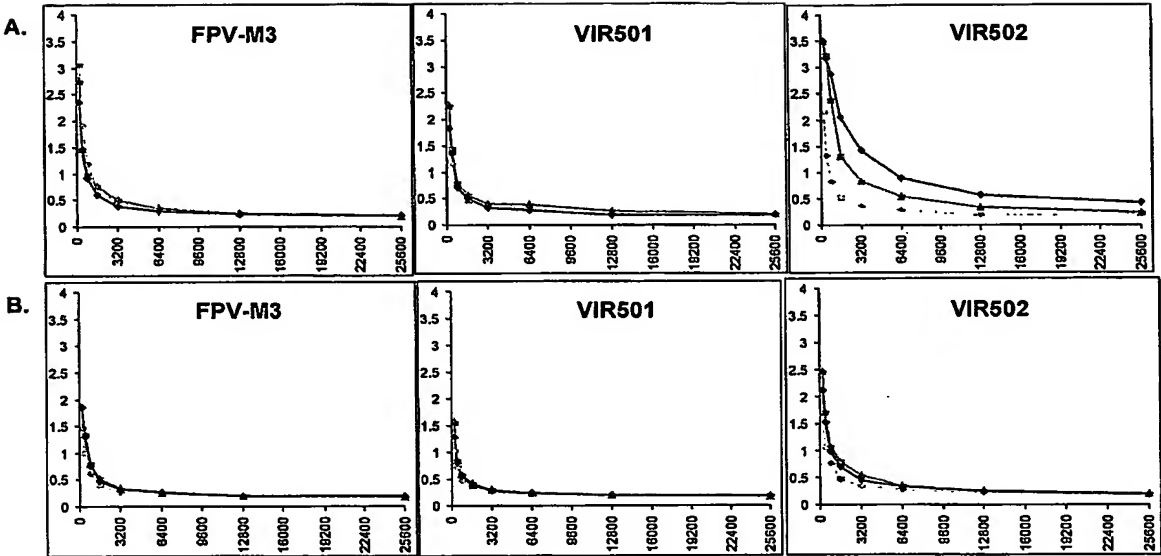


FIGURE 4

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Insertion site of VIR501 containing human IL2 and rat PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

ATGGATAGAAATATCAATTTTAGTCCTGTATTTATAGAACCTAGGTTTAAACACGAGTTTCTATTATCTCCTCAAAGGTATTTT
TACCTATCTTTATAGTTAAATCAGGACATAAATATCTTGGATCCAAATTTGTGCTCAAAGATAATAGAGGAGTTTCCATAAAA

TATATATTAGTTTTTGAAGTAATAGTAGCTTTGATTATATTGAATTTTTCTTTAAGGAAGAAATATTATATACATTTTTTCCG
ATATATAATCAAAACTTCATTATCATCGAACTAATATAACTTAAAAAGAAATTCCTTCTTTATAATATATGTAAAAAGGC
FPV132R ORF in bold →

TTAGCTAAGCCTTCTAAAAATTCAATAAATAGTCTGCTGGATAGAACTATGTTAAATGTGAAGAAGATGGATCTTTGATGATT
AATCGATTCCGAAGATTTTTAAGTTATTTATCAGACGACCTATCTTGATACAATTTTACACTTCTTCTACCTAGAACTACTAA

TCGAGACCTTCCGGTATCTATTCCGCCCTTGAGTTTAGATGGTTCACCGGTAAGGATTTCCGATTGTAGTTTGCTTTTATCGTCA
AGCTCTGGAAGGCCATAGATAAGCCGGAACCTCAAATCTACCAAGTGCCATTCTTAAAGGCTAACATCAAACGAAAATAGCAGT

ATAAATGGCGCATCCTCATCAACATCTCCTTACTCTATTTTTAAACAGACGATAACGGATTTTATTCCTTATCTATCCGAAAAAG
TATTTACCGCGTAGGAGTAGTTGTAGAGGAATGAGATAAAAAATGTCTGCTATTGCGCTAAAATAAGAATAGATAGGCTTTTTTC

TGATGATGAAGCTCTTGAAGACATAAATACTATTAAGAAATATATGGACTTTATTCTAAGCGTTCTTATACGTTCTAAAGAGAA
ACTACTACTTCGAGAACTTCTGTATTTATGATAATCTTTATATACCTGAAATAAGATTGCAAGAATATGCAAGATTTCTCTT

ACTAGAAAATATAGGATGTTCTTACGAGCCTATGAGTGAATCGTTTAAAGGCTCTTATTAAGTAAAGGATGATGGTACTTTAGT
TGATCTTTTATATCCTACAAGAATGCTCGGATACTCACTTAGCAAATTCGAGAAATAATTTCAATTTCTACTACCATGAAATCA

AAAAGCATTTACCAAGCCATTGTTAAATCCTCATTCCGAAAAGATAGTTTTAGATAGAGGTTATACCTCGGATTTTGCTATAAG
TTTTCGTAAATGGTTCGGTAACAATTTAGGAGTAAGGCTTTTCTATCAAATCTATCTCCAATATGAAGCCTAAAACGATATTC

CGTAATAAGACTATCTAGTAAAAGCAGTTATATACTTCCCGCAAATACAAAATACATAAATCCAAACGAGAATATGTATATAAA
GCATTATTCTGATAGATCATTTCGTCATATATGAAGGGCGTTTATGTTTTATGTATTTAGGTTTGCTCTTATACATATATTT

CAACCTAATATCACTACTGAAGCGCAACTAGATCTTCCAAACCCACCCGCTTTTTTATAGTAAGTTTTTCACCCATAAATAATAA
GTTGGATTATAGTGATGACTTCGCGTTGATCTAGAAGGTTTGGGTGGGCGAAAAATATCATTCAAAAAGTGGGTATTATTATT
vaccinia p7.5 promoter in bold & italic →

ATACAATAATTAATTTCTCGTAAAAGTAGAAAAATATATTCTAATTTATTGCACGGTCTAGAAGTAGTGgatccatGTACAGGAT
TATGTTATTAATTAAGAGCATTTCATCTTTTATATAAGATTAAATAACGTGCCAGATCTTGATCACctaggTACATGTCTTA
> M Y R M

GCAACTCCTGTCTTGCACTAATTCCTGCACTTGTCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAAACAAAGAA
CGTTGAGGACAGAACGTAACGTGATTAAGAACGTGAACAGTGTGTGTCACGTGGATGAAGTTCAAGCTGTTTCTTTGTTTCTT

> Q L L S C I A L I L A L V T N S A P T S S S T K K T K K
human IL2 protein coding sequence →

AACACAGCTACAACCTGGAGCATTTACTGCTGGATTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACCTCAC
TTGTGTCGATGTTGACCTCGTAAATGACGACCTAAATGTCTACTAAAACCTTACCTTAATTATTAATGTTCTTAGGGTTTGAGTG

> T Q L Q L E H L L L D L Q M I L N G I N N Y K N P K L T

CAGGATGCTCACATTTAAGTTTTACATGCCCAAGAAGGCCACAGAAGTGAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACC
GTCTTACGAGTGTAATTCAAAATGTACGGGTTCTTCCGGTGTCTTGACTTTGTGCAAGTCACAGATCTTCTTCTTGAGTTTGG

> R M L T F K F Y M P K K A T E L K Q L Q C L E E E L K P

TCTGGAGGAAGTGCTGAATTTAGCTCAAAGCAAAACCTTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGT
AGACCTCCTTCACGACTTAAATCGAGTTTCGTTTTTGAAAGTGAATCTGGGTCCCTGAATTAGTCGTTATAGTTGCATTATCA

> L E E V L N L A Q S K N F H L R P R D L I S N I N V I V

TCTGGAACATAAAGGGATCTGAAACAACATTCATGTGTGAATATGCAGATGAGACAGCAACCATTTGTAGAATTTCTGAACAGATG
AGACCTTGATTTCCCTAGACTTTGTTGTAAGTACACACTTATACGTCTACTCTGTCGTTGGTAACATCTTAAAGACTTGCTCTAC

> L E L K G S E T T F M C E Y A D E T A T I V E F L N R W

FIGURE 5

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GATTACCTTTTGTCAAAGCATCATCTCAACACTAAGTTGAT**TTTTTGT**aGATCTGTGAC**CATT**AGTATCCTAA**ATTGAA**
 CTAATGGAAACAGTTTCGTAGTAGAGTTGTGATTGA**ACTAAAAACA**tCTAGACAGCTG**GTAAATCATAGGATTTTA**ACTT
 > I T F C Q S I I S T L T . FPV early/late
 promoter

Early transcriptional
 stop sequence (bold)

TTGTAAATTATCGATAATAAATGAGAGCTGTCCCTCTGCACCTCGTCGGGACAGCAAGCCTCACCCCTTGGCTTCTTGCTCCTGCT
AACATTAATAGCTATTATTTACTCTCGACAGGGAGACGTGGAGCAGCCCTGTCGTTTCGGAGTGGGAACCGAAGAACGAGGACGA
 > M R A V P L H L V G T A S L T L G F L L L L
 Rat PAP protein coding sequence

ATCTCTCCGCCTGGACCCAGGCCAAGCCAAGGAGTTGAAGTTTGTGACATTGGTGTTCGGCATGGAGACCGAGGTCCCATCGA
 TAGAGAGGCGGACCTGGGTCCGGTTCGGTTCCTCAACTTCAAACACTGTAACCAAGGCCGTACCTCTGGCTCCAGGGTAGCT
 > S L R L D P G Q A K E L K F V T L V F R H G D R G P I E

GACCTTTCCTAATGACCCATTAAAGGAATCCTCGTGGCCACAAGGATTTGGCCAACTCACCAAGTGGGGCATGGGACAGCACTA
 CTGGAAAGGATTACTGGGGTAATTCCTTAGGAGACCGGTGTTCTAAACCGTTGAGTGGTTCACCCCGTACCTGTCTGTGAT
 > T F P N D P I K E S S W P Q G F G Q L T K W G M G Q H Y

CGAACTCGGAAGTTATATAAGGAGAAGATACGGGAGATTCTTGAACAACCTCTATAAACATGACCAGGTTTATATCCGAAGCAC
 GCTTGAGCCTTCAATATATTCTTCTATGCCCTCTAAGAACTTGTGAGGATATTTGTACTGGTCCAAATATAGGCTTCGTG
 > E L G S Y I R R R Y G R F L N N S Y K H D Q V Y I R S T

AGATGTTGACAGGACTCTGATGAGCGCTATGACAAACCTCGCAGCCCTGTTTCCCCCTGAGGGGATCAGCATCTGGAATCCCAG
 TCTACAACCTGTCTGAGACTACTCGCGATACTGTTTGGAGCGTCGGGACAAAGGGGGACTCCCCTAGTCGTAGACCTTAGGGTC
 > D V D R T L M S A M T N L A A L F P P E G I S I W N P R

ACTGCTCTGGCAGCCCATCCAGTGACACCGTGTCTCTCTCTGAGGATCGGTGCTATACCTGCCTTTCAGGGACTGTCTCTCG
 TGACGAGACCGTCGGGTAGGGTCACGTGTGGCACAGAGAGACTCCTAGCCAACGATATGGACGGAAAGTCCCTGACAGGAGC
 > L L W Q P I P V H T V S L S E D R L L Y L P F R D C P R

CTTCAAGAAGTCAAGAGTGAGACTTTAAATCTGAGGAGTTCCTGAAGAGGCTTCAACCATATAAAAGCTTCATAGACACCTT
 GAAAGTTCTTGAGTTCTCACTCTGAAATTTAGACTCCTCAAGGACTTCTCCGAAGTTGGTATATTTTCGAAGTATCTGTGGAA
 > F Q E L K S E T L K S E E F L K R L Q P Y K S F I D T L

GCCATCGCTGTTCGGGATTCGAGGACCAGGATCTTTTTGAAATCTGGAGTAGGCTTTACGACCCCTTTATATTGCGAGAGTGTTC
 CGGTAGCGACAGCCCTAAGCTCCTGGTCCTAGAAAACTTTAGACCTCATCCGAATGCTGGGAAATATAACGCTCTCACAAGT
 > P S L S G F E D Q D L F E I W S R L Y D P L Y C E S V H

CAATTTACCTTCCGCACCTGGGCCACAGAGGACGCCATGACTAAGTTGAAGGAGTTGTCAGAATTATCTCTGTTATCTCTTTA
 GTTAAAGTGGAAGCGTGGACCCGGTGTCTCCTGCGGTACTGATCAACTTCCTCAACAGTCTTAATAGAGACAATAGAGAAAT
 > N F T F R T W A T E D A M T K L K E L S E L S L L S L Y

TGGAATTCAAGCAGAAAGAGAAATCTAGACTCCAGGGGGGCGTCTGGTCAATGAAATTTCTCAAGAACATGAAGCTTGCAAC
 ACCTTAAGTGTTCGTCTTTCTCTTTAGATCTGAGGTCCCCCGCAGGACAGTTACTTTAAGAGTTCTTGTAAGTCTCGAACGTTG
 > G I H K Q K E K S R L Q G G V L V N E I L K N M K L A T

TCAACCACAGAAGGCCAGGAAGTTGATCATGTATTCTGCATATGACACTACTGTGAGTGGCCTGCAGATGGCGCTAGAGCTTTA
 AGTTGGTGTCTTCCGGTCTTCAACTAGTACATAAGACGTATACGTGATGACACTCACCAGGACGTCTACCGCATCTCGAAAT
 > Q P Q K A R K L I M Y S A Y D T T V S G L Q M A L E L Y

TAATGGACTTCTACCTCCCTACGCTTCTGCCCACATAATGGAATGTACCAGGATAATGGGGGGACCTTCGTGGAGATGTACTA
 ATTACCTGAAGATGGAGGATGCGAAGGACGGTGTATTACCTTAACATGGTCTTATTACCCCTTGAAGCACCTCTACATGAT
 > N G L L P P Y A S C H I M E L Y Q D N G G T F V E M Y Y

CCGGAATGAGACCCAGAACGAGCCCTACCCACTCACGCTGCCGGGTGTACCCACAGCTGCCCTCTGGAGAAGTTGCAGAGCT
 GGCTTACTCTGGGTCTTGCTCGGGATGGGTGAGTGCACGGCCCGACATGGGTGTGACGGGAGACCTCTTCAAACGCTCTCGA
 > R N E T Q N E P Y P L T L P G C T H S C P L E K F A E L

FIGURE 5 cont.

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ACTGGACCCCGTGATCCCCAGGACTGGGCCACAGAGTGATGGGCACAAGCAACCACCAAGCGTCGCTGTAATTTTTCTGTCTG
TGACCTGGGGCACTAGGGGGTCCTGACCCGGTGTCTCACATACCCGTGTTGTTGGTGGTTCGCAGCGACATTAAAAAGACAGC
> L D P V I P Q D W A T E C M G T S N H Q A S L .

ACCCATGGTTGTTAAAAAGGAATTGAAAGAAAATATTTTATATCGTAATAAATTAAATATGCATGAAGGACATCAGGAGTCTTT
TGGGTACCAACAATTTTTCCTTAACTTTCTTTTATAAAATATAGCATTATTTAATTTATACGTACTTCCTGTAGTCCTCAGAAA
FPV134R ORF in bold

TAAAGAACTTGAAATGACAAAACCTTATATGTTCTTCAATGAACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTC
ATTTCTTGAACTTTACTGTTTTGGAATATACAAGAAGTTACTTGATCATCCACTTCTTCTGATATTGTTTCTCAATCTTTTAAG

TAATACTAAGTTTCAAGGACAGGGCCAGCTTAAGCTGTTATTAGGAGAAGTTTATTTCTTAAATACATTAATCAAGAATAAAAC
ATTATGATTCAAAGTTCTGTCCCGGTCGAATTCGACAATAATCCTCTTGAAATAAAGAATTTATGTAATTAGTTCTTATTTTG

GTTATGTTTCAATACAGTTATCGTGTATATAGGGTCAGCACCAGGAAGCCATATAAAATTTTATATcATTATATGGATGA
CAATACAAGTCTATGTCAATAGCACATATATCCAGTCGTGGTCCTTCGGTATATTTAAAAATA **TA** **AGTAATATACCTACT**
Early transcriptional
stop sequence for rat PAP

TCTTAAATAGATTTAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTCTAGAAAGTCTTAAATGTGTCTATAAT
AGAATTTTATCTAAATTTTACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTTCAGAATTTTACACAGATATTA

ACATAGGTTTGTAGATGAACAATACTTGTTTAAAGCTACGTAATATGATTAGGAAAAACATAAAATTGTACTGATATCAGATAT
TGTATCCAAACATCTACTTGTTATGAACAAATTCGATGCATTATACTAATCCTTTTGGTATTTTAACATGACTATAGTCTATA

TAGATCGCTAAGAGGAAAAGAACCTACTAGCGAGGACCTATTACACGATTACGCGTTGCAGAATCAAATGGTAAGCATTCTTAA
ATCTAGCGATTCTCCTTTTCTTGGATGATCGCTCCTGGATAATGTGCTAATGCGCAACGTCTTAGTTTACCATTTCGTAAGAATT

ACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTTCCGGATCAGTGGATAAGAGACTTTTACATTCCTTGTGGAGATGAGTT
TGGTTATCGTAGCTCGGACTTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTCTGAAAATGTAAGGAACACCTCTACTCAA

T
A

FIGURE 5 cont.

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Insertion site of VIR502 containing human IL2 and human PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

**ATGGATAGAAATATCAATTTTAGTCCGTATTTATAGAACCTAGGTTTAAACACGAGTTTCTATTATCTCCTCAAAGGTA
TACCTATCTTTATAGTTAAAATCAGGACATAAATATCTTGGATCCAAATTTGTGCTCAAAGATAATAGAGGAGTTTCCAT**
FPV132R ORF in bold →

**TTTTTATATATTAGTTTTTGAAGTAATAGTAGCTTTGATTATATTGAATTTTTTCTTTAAGGAAGAAATATTATATACAT
AAAAATATATAATCAAAAACCTTCATTATCATCGAACTAATATAACTTAAAAAGAAATTCCTTCTTTATAATATATGTA**

**TTTTTCCGTTAGCTAAGCCTTCTAAAAATCAATAAATAGTCTGCTGGATAGAACTATGTTAAATGTGAAGAAGATGGA
AAAAAGGCAATCGATTCTGGAAGATTTTTAAGTTATTTATCAGACGACCTATCTTGATACAATTTTACACTTCTTCTACCT**

**TCTTGATGATTTTCGAGACCTTCCGGTATCTATTCCGGCTTGAGTTTAGATGGTTCACCGGTAAGGATTTCCGATTGTAG
AGAACTACTAAAGCTCTGGAAGGCCATAGATAAGCCGGAACCTCAAATCTACCAAGTGGCCATTCTTAAAGGCTAACATC**

**TTTGCTTTTATCGTCAATAAATGGCGCATCTCATCAACATCTCCTTACTCTATTTTAAACAGACGATAACGGATTTTAT
AACGAAAATAGCAGTTATTTACCGCGTAGGAGTAGTTGTAGAGGAATGAGATAAAAAATTGTCTGCTATTGCCTAAAATA**

**TCTTATCTATCCGAAAAAAGTGATGATGAAGCTCTTGAAGACATAAATACTATTAAGAAATATATGGACTTTATTCTAAG
AGAATAGATAGGCTTTTTTCACTACTACTTCGAGAACCTCTGTATTTATGATAATCTTTATATACCTGAAATAAGATTC**

**CGTTCCTTATACGTTCTAAAGAGAACTAGAAAATATAGGATGTTCTTACGAGCCTATGAGTGAATCGTTAAGGCTCTTA
GCAAGAATATGCAAGATTTCTCTTTGATCTTTTATATCCTACAAGAATGCTCGGATACTCACTTAGCAAATTCGAGAAT**

**TTAAAGTAAAGGATGATGGTACTTTAGTAAAAGCATTTACCAAGCCATTGTTAAATCCTCATTCGAAAAGATAGTTTTTA
AATTTCAATTCCTACTACCATGAAATCATTTTCGTAAATGGTTCGGTAAACAATTTAGGAGTAAGGCTTTTCTATCAAAAT**

**GATAGAGGTTATACCTTCGGATTTTGTCTATAAGCGTAATAAGACTATCTAGTAAAAGCAGTTATATACTTCCCGCAAATAC
CTATCTCCAATATGAAGCCTAAAACGATATTCGCATTATTCTGATAGATCATTTTCGTCAATATATGAAGGGCGTTATG**

**AAAATACATAAATCCAAACGAGAATATGTATATAAACACCTAATATCACTACTGAAGCGCAACTAGATCTTCCAAACCC
TTTTATGTATTTAGGTTTGCTCTTATACATATATTTGTTGGATTATAGTGATGACTTCGCGTTGATCTAGAAGGTTTGGG**

**ACCCGCTTTTATAGTAAGTTTTTACCCATAAAATAAATAACAATAATTAATTTCTCGTAAAGTAGAAAATATATTC
TGGGCGAAAAATATCATTCAAAAAGTGGGTATTATTATTATGTTATTAATTAAGAGCATTTTCATCTTTTATATAAG**
vaccinia p7.5 promoter in bold & italic →

**TAATTTATTGCACGGTCTAGAACTAGTGgatccATGTACAGGATGCAACTCCTGTCTTGCAATGCACTAATCTTGCACT
ATTAAATAACGTGCCAGATCTTGATCACctaggTACATGTCCTACGTTGAGGACAGAACGTAACGTGATTAAGAACGTGA**

> M Y R M Q L L S C I A L I L A L

Human IL2 protein coding sequence →

**TGTCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAAAACAGCTACAACCTGGAGCATTTACTGCTGG
ACAGTGTGTTGTACGTGGATGAAGTTCAAGCTGTTTCTTTTGTTCCTTTGTGTCGATGTTGACCTCGTAAATGACGACC**
> V T N S A P T S S S T K K T K K T Q L Q L E H L L L

**ATTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACCTCACCAGGATGCTCACATTTAAGTTTTACATG
TAAATGTCTACTAAAACCTTACCTTAATTATTAATGTTCTTAGGGTTGAGTGGTCTACGAGTGTAATTCAAAATGTAC**
> D L Q M I L N G I N N Y K N P K L T R M L T F K F Y M

**CCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTAGC
GGGTTCTCCGGTGTCTTGACTTTGTGCAAGTCACAGATCTTCTTGTGAGTTTGGAGACCTCCTTCACGACTTAAATCG**
> P K K A T E L K Q L Q C L E E L K P L E E V L N L A

**TCAAAGCAAAAACCTTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGTTCTGGAACATAAAGGGATCTG
AGTTTCGTTTTTGAAGTGAATCTGGGTCCCTGAATTAGTCGTTATAGTTGCATTATCAAGACCTTGATTTCCCTAGAC**
> Q S K N F H L R P R D L I S N I N V I V L E L K G S

FIGURE 6

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AAACAACATTCATGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAACAGATGGATTACCTTTTGTCAA
TTTGTGTAAGTACACACTTATACGTCTACTCTGTCGTTGGTAACATCTTAAAGACTTGTCTACCTAATGGAAAACAGTT
> E T T F M C E Y A D E T A T I V E F L N R W I T F C Q

AGCATCATCTCAACACTAACTTGA**TTTTTGT**aGATCTGtcgaccatttagtatcctaaaattgaattgtaattatcg
TCGTAGTAGAGTTGTGATTGAACT**AAAAACA**tCTAGACagctggtaaatcataggattttaacttaacattaatago
> S I I S T L T . FPV early late promoter →
Early transcriptional in bold & italic
stop sequence in bold

ataataaATGAGAGCTGCACCCCTCCTCCTGGCCAGGGCAGCAAGCCTTAGCCTTGGCTTCTTGTTTCTGCTTTTTTTTCT
tattattACTCTCGACGTGGGGAGGAGGACCGGTCCCGTCGTTCCGAATCGGAACCGAAGAACAAGACGAAAAAAGA
> M R A A P L L L A R A A S L S L G F L F L L F F
Human PAP protein coding sequence →

GGCTAGACCGAAGTGTACTAGCCAAGGAGTTGAAGTTTGTGACTTTGGTGTTCGGCATGGAGACCGAAGTCCCATTGAC
CCGATCTGGCTTCACATGATCGGTTCCCTCAACTTCAAACACTGAAACCACAAAGCCGTACCTCTGGCTTCAGGGTAAC TG
> W L D R S V L A K E L K F V T L V F R H G D R S P I D

ACCTTTCCCACTGACCCCATAAAGGAATCCTCATGGCCACAAGGATTTGGCCAACTACCCAGCTGGGCATGGAGCAGCA
TGGAAAGGGTGACTGGGGTATTTCCCTAGGAGTACCGGTGTTCTAAACCGGTTGAGTGGGTGACCCGTACCTCGTCGT
> T F P T D P I K E S S W P Q G F G Q L T Q L G M E Q H

TTATGAACCTGGAGAGTATATAAGAAAGAGATATAGAAAATCTTGAATGAGTCCATATAACATGAACAGGTTTATATTC
AATACTTGAACCTCTCATATATTCTTCTCTATATCTTTTAAGAACTTACTCAGGATATTTGTACTTGTCCAATATAAG
> Y E L G E Y I R K R Y R K F L N E S Y K H E Q V Y I

GAAGCACAGACGTTGACCGGACTTTGATGAGTGCTATGACAAACCTGGCAGCCCTGTTTCCCCAGAAGGTGTGACATC
CTTCGTGTCTGCAACTGGCCTGAACTACTCACGATACTGTTTGGACCGTCGGGACAAAGGGGGTCTTCCACAGTCGTAG
> R S T D V D R T L M S A M T N L A A L F P P E G V S I

TGGAATCCTATCCTACTCTGGCAGCCCATCCCGGTGCACACAGTTCCCTCTTCTGAAGATCAGTTGCTATACCTGCCTTT
ACCTTAGGATAGGATGAGACCGTCGGGTAGGGCCACGTGTCTCAAGGAGAAAGACTTCTAGTCAACGATATGGACGGAAA
> W N P I L L W Q P I P V H T V P L S E D Q L L Y L P F

CAGGAAGTGGCCCTCGTTTCAAGAACTTGAGAGTGAGACTTTGAAATCAGAGGAATTCCAGAAGAGGCTGCACCCCTTATA
GTCCCTTGACGGGAGCAAAAGTTCTTGAACCTCACTCTGAACTTTAGTCTCCTTAAGGTCTTCTCCGACGTGGGAATAT
> R N C P R F Q E L E S E T L K S E E F Q K R L H P Y

AGGATTTTATAGCTACCTTGGGAAAACTTTCAGGATTACATGGCCAGGACCTTTTGGAAATTTGGAGTAAAGTCTACGAC
TCCTAAAATATCGATGGAACCCCTTTTGAAGTCCTAATGTACCGGTCTGGAAAACCTTAAACCTCATTTTCAGATGCTG
> K D F I A T L G K L S G L H G Q D L F G I W S K V Y D

CCTTTATATTGTGAGAGTGTTTACAAATTTCACTTTACCCTCCTGGGCCACTGAGGACACCATGACTAAGTTGAGAGAATT
GGAAATATAACACTCTCACAAGTGTTAAAGTGAAATGGGAGGACCCGGTACTCCTGTGGTACTGATTCAACTCTCTTAA
> P L Y C E S V H N F T L P S W A T E D T M T K L R E L

GTCAGAATTGTCCCTCCTGTCCCTCTATGGAATTCACAAGCAGAAAGAGAAATCTAGGCTCCAAGGGGGTGTCTGGTCA
CAGTCTTAACAGGGAGGACAGGGAGATACCTTAAGTGTTCTGTTCTTTCTTTAGATCCGAGGTTCCCCACAGGACCACT
> S E L S L L S L Y G I H K Q K E K S R L Q G G V L V

ATGAAATCCTCAATCACATGAAGAGAGCAACTCAGATACCAAGCTACAAAAAATTTATCATGTATTCTGCGCATGACACT
TACTTTAGGAGTTAGTGACTTCTCTCGTTGAGTCTATGGTTCGATGTTTTTTGAATAGTACATAAGACGCGTACTGTGA
> N E I L N H M K R A T Q I P S Y K K L I M Y S A H D T

ACTGTGAGTGGCCTACAGATGGCGCTAGATGTTTACAACGGACTCCTTCTCCCTATGCTTCTTGGCACTTGACGGAATT
TGCACTCACCGGATGTCTACCGGATCTACAAATGTTGCCGTGAGGAAGGAGGGATACGAAGAAGGTGAACTGCCTTAA
> T V S G L Q M A L D V Y N G L L P P Y A S C H L T E L

FIGURE 6 cont.

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GTACTTTGAGAAGGGGGAGTACTTTGTGGAGATGTACTATCGGAATGAGACGCAGCACGAGCCGTATCCCCTCATGCTAC
CATGAAACTCTTCCCCCTCATGAAACACCTCTACATGATAGCCTTACTCTGCGTCGTGCTCGGCATAGGGGAGTACGATG
> Y F E K G E Y F V E M Y Y R N E T Q H E P Y P L M L

CTGGCTGCAGCCCTAGCTGTCTCTGGAGAGGTTTGTGAGCTGGTTGGCCCTGTGATCCCTCAAGACTGGTCCACGGAG
GACCGACGTCGGGATCGACAGGAGACCTCTCAAACGACTCGACCAACCGGACACTAGGGAGTTCTGACCAGGTGCCTC
> P G C S P S C P L E R F A E L V G P V I P Q D W S T E

TGTATGACCACAAACAGCCATCAAGGTACTGAGGACAGTACAGATTAATTTTTCTGTCGACCCATGGTTGTTAAAAAGGA
ACATACTGGTGGTTGTGCGGTAGTTCCATGACTCCTGTCTATGTCTAATTAATAAGACAGCTGGGTACCAACAATTTTCTCT
> C M T T N S H Q G T E D S T D •

ATTGAAAGAAAATATTTTATATCGTAATAAATTAAATATGCATGAAGGACATCAGGAGTCTTTTAAAGAACTTGAAATGA
TAACCTTTCTTTTATAAAATATAGCATTATTTAATTTATACGTACTTCTGTAGTCCTCAGAAAATTTCTTGAACCTTTACT
FPV134 ORF in bold →

CAAAACCTTATATGTTCTTCAATGAAC TAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTC TAATACTAAGTTT
GTTTTGGAATATACAAGAAGTTACTTGATCATCCACTTCTCTGATATTGTTTCTCAATCTTTTAAGATTATGATTCAAA

CAAGGACAGGGCCAGCTTAAGCTGTTATTAGGAGAAGCTTTATTTCTTAAATACATTAATCAAGAATAAAACGTTATGTTT
GTTCTGTCCCGGTCGAATTCGACAATAATCCTCTTGAATAAAGAATTTATGTAATTAGTTCTTATTTTGAATACAAG

AGATACAGTTATCGTGTATATAGGGTCAGCACCAGGAAGCCATATAAATTTTTTTATATCATTATATGGATGATCTTA
TCTATGTCAATAGCACATATATCCAGTCGTGGTCCTTCGGTATATTTTAAAAATA TAGTAATATACCTACTAGAAT

Early transcriptional
stop sequence in bold
for human PAP sequence

AAATAGATTTAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTCTAGAAAAGTCTTAAAAATGTGTCTATAATA
TTTATCTAAATTTTACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTTCAGAATTTTACACAGATATTAT

CATAGGTTTGTAGATGAACAATACTTGTTTAAAGCTACGTAATATGATTAGGAAAACCATAAAATGTACTGATATCAGA
GTATCCAAACATCTACTTGTTATGAACAAATTCGATGCATTATACTAATCCTTTTGGTATTTTAACATGACTATAGTCT

TATTAGATCGCTAAGAGGAAAAGAACC TACTAGCGAGGACCTATTACACGATTACGCGTTGCAGAATCAAATGGTAAGCA
ATAATCTAGCGATTCTCCTTTTCTTGGATGATCGCTCCTGGATAATGTGCTAATGCGCAACGCTCTTAGTTTACCATTTCGT

TTCTTAAACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTCCGGATCAGTGGATAAGAGACTTTTACATTCCCTTGT
AAGAATTTGGTTATCGTAGCTCGGACTTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTCTGAAAATGTAAGGAACA

GGAGATGAGTTT
CCTCTACTCAA

FIGURE 6 cont.

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Amino acid sequence alignment of rat PAP from VIR501 with human PAP from VIR502

Boxed: Identical amino acid

| | | | | |
|-----|---|-----------------|----------------|-----|
| | 10 | 20 | 30 | |
| 1 | M R A V P L H L V G T A S I T L G F L L L I S L R L D P G D | A K E L K F V T | LratPAP aa seq | |
| 1 | M R A A P L L L A R A A S I S L G F L L L I F F W L D R S V | A K E L K F V T | LhuPAP aa seq | |
| | 40 | 50 | 60 | 70 |
| 40 | V F R H G D R G P I E T F P N D P I K E S S W P Q G F G Q L T K W G M G Q H Y | EratPAP aa seq | | |
| 41 | V F R H G D R S P I D T F E T D P I K E S S W P Q G F G O L T Q L G M E O H Y | EhuPAP aa seq | | |
| | 80 | 90 | 100 | 110 |
| 80 | L G S Y I R R R Y G R F L N N S Y K H D Q V Y I R S T D V D R T L M S A M T N | LratPAP aa seq | | |
| 81 | L G E Y I R K R Y R K F L N E S Y K H E O V Y I R S T D V D R T L M S A M T N | LhuPAP aa seq | | |
| | 120 | 130 | 140 | 150 |
| 120 | A A L F P P E G I S I W N P R L L W Q P I P V H T V S L S E D R L L Y L P F R | DratPAP aa seq | | |
| 121 | A A L F P P E G V S I W N E T L L W O P I P V H T V R L S E D Q L L Y L P F R | NhuPAP aa seq | | |
| | 160 | 170 | 180 | 190 |
| 160 | C P R F Q E L K S E T L K S E E F L K R L O P Y K S F I D T L P S L S G F E D | QratPAP aa seq | | |
| 161 | C P R F O E L E S E T L K S E E F L K R L H P Y K D F I A T L G K L S G L H G | QhuPAP aa seq | | |
| | 200 | 210 | 220 | 230 |
| 200 | D L F E I W S R L Y D P L Y C E S V H N F T F R T W A T E D A M T K L K E L S | EratPAP aa seq | | |
| 201 | D L F G I W S K V Y D P L Y C E S V H N F T L P S W A T E D T M T K L R E L S | EhuPAP aa seq | | |
| | 240 | 250 | 260 | 270 |
| 240 | L S L L S L Y G I H K Q K E K S R L Q G G V L V N E I L K N M K L A T O P O K | AratPAP aa seq | | |
| 241 | L S L L S L Y G I H K Q K E K S R L O G G V L V N E I L N M K R A T D I P S | YhuPAP aa seq | | |
| | 280 | 290 | 300 | 310 |
| 280 | R K L I M Y S A Y D T T V S G L Q M A L E I Y N G L L P P Y A S C H I M E L Y | QratPAP aa seq | | |
| 281 | K K L I M Y S A H D T T V S G L O M A L D V Y N G L L P P Y A S C H L T E L Y | FhuPAP aa seq | | |
| | 320 | 330 | 340 | 350 |
| 320 | D N G G T F V E M Y Y R N E T Q N E P Y P L T L P G C T H S C P L E K F A E L | LratPAP aa seq | | |
| 321 | E K G E Y F V E M Y Y R N E T C H E P Y P L N L P G C S P S C P L E R F A E L | VhuPAP aa seq | | |
| | 360 | 370 | 380 | |
| 360 | D P V I P Q D W A T E C M G T S N H Q A S T | ratPAP aa seq | | |
| 361 | G P V I P O D W S T E C M T T N S H O G T E D S T D | huPAP aa seq | | |

Decoration 'Decoration #1': Box residues that match ratPAP aa seq exactly.

FIGURE 7

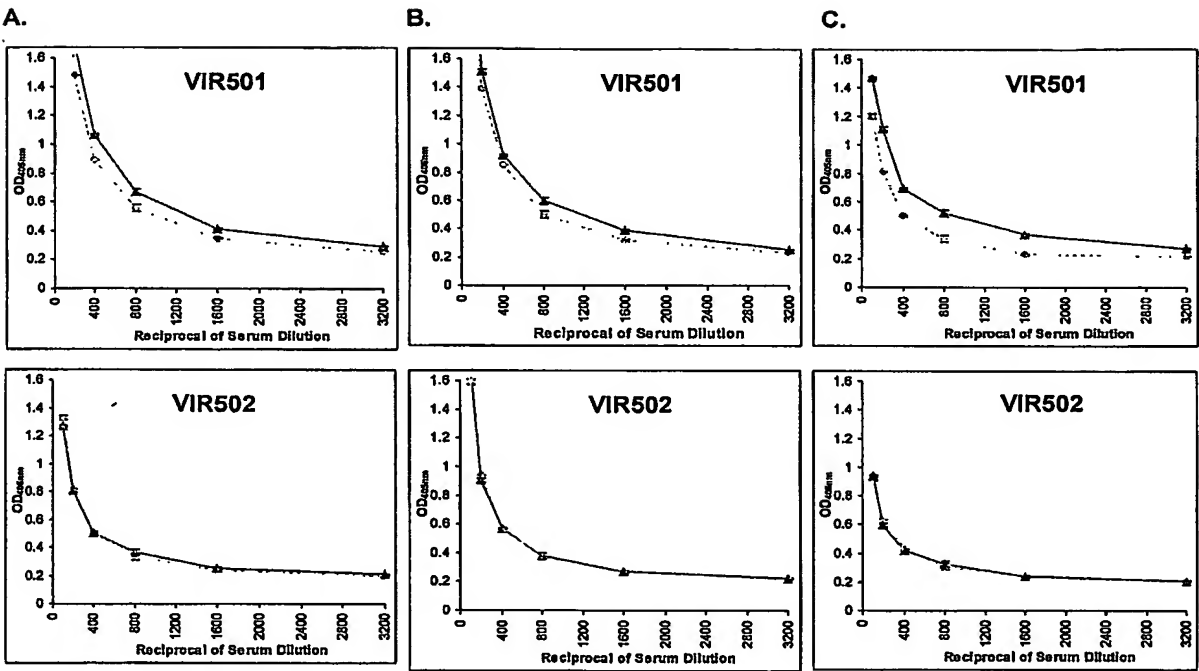


FIGURE 8

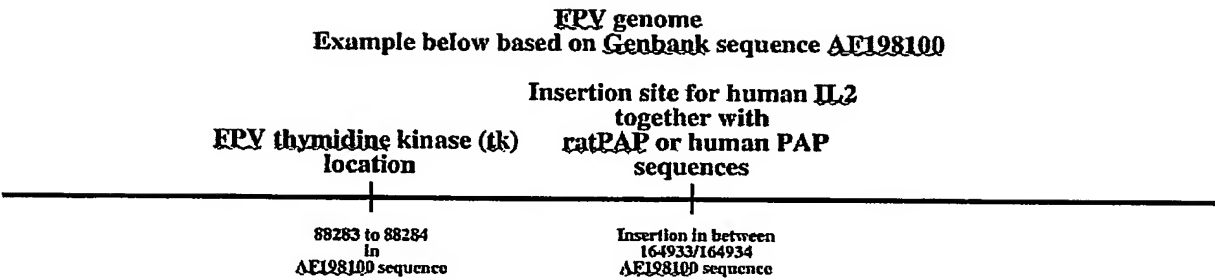
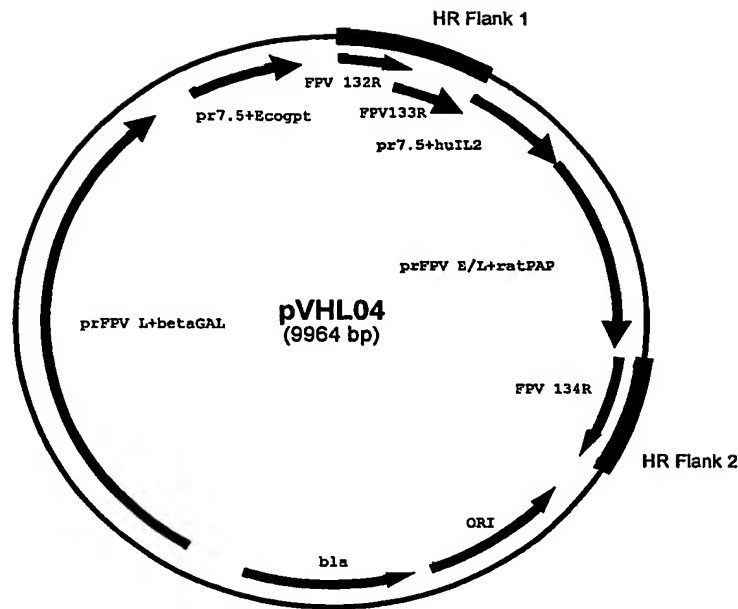


FIGURE 9

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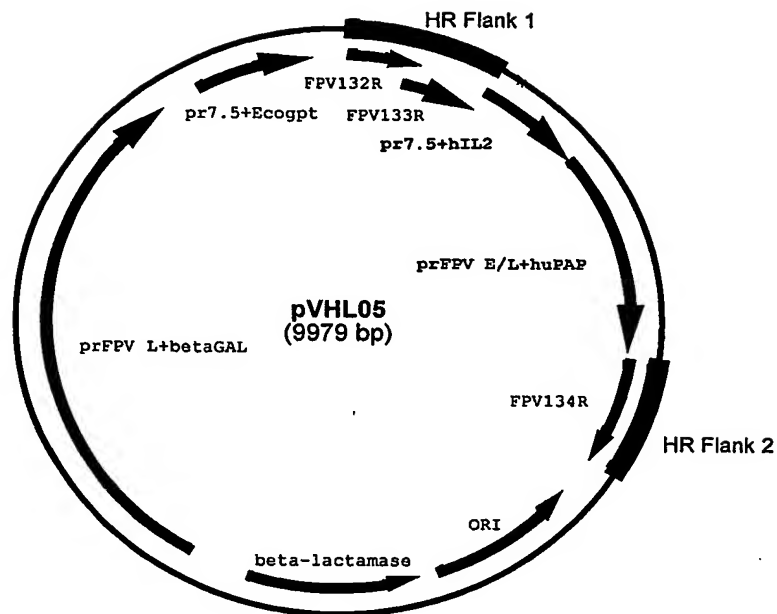


pVHL04 was constructed by cloning the following into a bacterial plasmid vector:

1. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
2. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
3. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs overlap each other. This sequence forms the homologous recombination flank 1.
4. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
5. prFPV E/L+rat PAP: rat prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
6. Fowlpox Virus nucleotide sequence spanning ORFs 134 – this sequence forms the homologous recombination flank 2.

FIGURE 10

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pVHL05 was constructed by cloning the following into a bacterial plasmid vector:

7. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
8. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
9. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs overlap each other. This sequence forms the homologous recombination flank 1.
10. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
11. prFPV E/L+huPAP: human prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
12. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

FIGURE 11